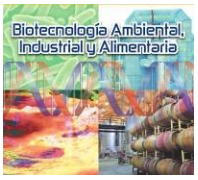
Poster



Optimization of brain organoids as models for the study of neurodegenerative diseases

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ABSTRACT

Motivation: One of the current challenges faced by neuroscience is the limited availability of in vitro models of neurodegenerative diseases, as there are notable anatomical and molecular differences among murine and human brain. As a result, significant efforts have been made towards the development of new models based on human cells, with cerebral organoids standing out as a particularly promising approach. Brain organoids are 3D models usually developed from induced pluripotent stem cells (iPSCs) that simulate the composition and cytoarchitecture of different regions of the human brain. They may allow us to obtain in vitro information about the human brain, which makes them a valuable model for investigating neurodegenerative diseases. Nevertheless, they present disadvantages associated with the absence of essential components for their development and functionality. Therefore, we will investigate the effect of incorporating an extracellular matrix (ECM) from human and pig brain into the culture of these organoids, as it contains specific combinations of components that play a role in multiple neuronal processes. On the other hand, in order to find the optimal model for generating this organoids, two protocols, Lancaster (1) and Rosebrock (2), have been compared. Lancaster's protocol is the most cited for brain organoids, but following it, other embryonic layers are developed. Rosebrock's protocol, is a modification of the Lancaster's protocol, in which SMAD pathway inhibitors are used to avoid the formation of non-ectodermal layers.

Methods: We generated brain organoids from iPSC, following two protocols: Lancaster (1) and Rosebrock (2). Two ECM conditions were used during cultures: Matrigel versus ECM obtained from pig brain. Subsequently, the addition of human ECM will be tested. Finally, organoids are being characterized using different techniques such as immunofluorescence, RT-PCR and expression arrays.

Results: We have found molecular differences among brain organoids obtained following the different protocols, as those obtained following Rosebrock's protocol express fewer endodermal and mesodermal markers than those obtained with Lancaster's protocol. As well, we have identified different features between those organoids matured with ECM and those matured only with Matrigel, the former being larger than the latter. Further studies will discern whether there are other relevant differences between the models.

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